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RESEARCH DESIGN AND METHODS

Study population

The study population was men and women aged 30 to 65 years, who participated in the 9-year follow-up study, Data from an Epidemiological Study on the Insulin Resistance syndrome (D.E.S.I.R.) (2). Participants were recruited from volunteers attending free-of-charge health examinations, provided by the French Social Security, and recruited from 10 health examinations centres in western France. All subjects signed an informed consent and the protocol was approved by an ethics committee.

Participants were examined with biologic tests at inclusion, and every three years, over nine years.

Incident cases of diabetes were identified by

A. treatment for diabetes at one of the three-yearly examinations in 1896 men and 1976 women not treated for diabetes at baseline;
B. fasting plasma glucose (FPG) 7.0 mmol/l, at one of the three-yearly examinations in the 1846 men and 1944 women not treated for diabetes at baseline and with baseline FPG < 7.0 mmol/l;
C. HbA1c 6.5 %, at one of the three-yearly examinations in the 1849 men and 1940 women not treated for diabetes at baseline and with baseline HbA1c < 6.5 %;
D. FPG 7.0 mmol/l, and/or HbA1c 6.5 %, at one of the three-yearly examinations in the 1857 men and 1943 women not treated for diabetes at baseline and with baseline FPG < 7.0 mmol/l and HbA1c < 6.5 %;
E. treatment for diabetes and/or a FPG 7.0 mmol/l at one of the three-yearly examinations in the 1867 men and 1958 women, not treated for diabetes at baseline and with baseline FPG < 7.0 mmol/l;
F. treatment for diabetes and/or HbA1c 6.5 % at one of the three-yearly examinations in the 1874 men and 1954 women not treated for diabetes at baseline and with baseline HbA1c < 6.5 %;
G. treatment for diabetes and/or FPG 7.0 mmol/l and/or HbA1c 6.5 % at one of the three-yearly examinations in the 1878 men and 1958 women not treated for diabetes at baseline and with baseline FPG < 7.0 and HbA1c < 6.5 %.

All individuals studied had baseline data available for glucose, HbA1c, BMI and waist circumference. Missing data for other variables were replaced by the mean value; values were imputed for at most nine individuals.

In comparison to the 3825 men and women studied, for the definition of diabetes: FPG 7.0 mmol/l and/or treatment, the 1143 who were not able to be followed for the 9 years of the study were, at baseline, two years younger (45 vs 47 years), more were current smokers (32% vs 19%), more had hypertension (39% vs 35%) (all $P < 0.008$); both groups had the same mean FPG of 5.3 mmol/l at inclusion.

Measures

Two measures of blood pressure were taken in a supine position after 5 minutes rest; mean values were used. Weight and height were measured in lightly clad participants, and BMI calculated. The waist circumference, the smallest circumference between the lower ribs and the iliac crests, was also measured.

The examining physician noted the family history of diabetes, as well as treatment for diabetes, hypertension and lipids. Hypertension was defined by systolic and/or diastolic blood pressures of at least 140 and/or 90 mmHg and/or being on antihypertensive medication. Smoking habits, alcohol intake (consumption per day of wine, beer, cider and spirits) and degree of physical activity (at home, at work and sport) were assessed using a self-administered questionnaire. Alcohol consumption was classed according to pure alcohol intake as: zero, under 20 g/day, 20 to under 40 g/day, 40 g/day or above, and physical activity in two classes, sedentary versus some activity.

All biochemical measurements were from one of four health-centre biological laboratories located in France at Blois, Chartres, La Riche or Orléans. Fasting plasma glucose, was measured by the glucose-oxidase method in fluoro-oxalated plasma using a Technicon RA100 (Bayer Diagnostics, Puteaux, France) or a Specific or a Delta device (Konelab, Evry, France). HbA1c was quantified by High Performance Liquid Chromatography using a L9100 automated ion-exchange analyser (Hitachi/ Merck-VWR, Fontenay-sous-Bois) or a Radiant 1 (Bio-rad, Marne la Coquette, France), or by Immunoassay using a DCA2000 (Bayer Diagnostics, Puteaux, France). FPG and HbA1c have been standardized over laboratories and time periods, according to gender and age.

Statistical methods

Statistical analyses used SAS Version 9.1 (SAS Institute Inc. Cary, NC USA).

Participants included in the analysis were compared with those not able to be followed for the 9 years of the study, using the most classical definition of diabetes: FPG 7.0 mmol/l and/or treatment for diabetes, by t- and by ² tests.

Men and women not treated for diabetes at baseline, were characterised by means (SDs) or percentages, and compared by t- and ² tests, according to whether they were treated or not for diabetes after 9 years of follow-up.

Mean FPG and HbA1c were determined by age group, and the gender-age interaction was tested in a linear regression model including gender and age, using a statistical significance level of $P < 0.05$.

For each of the seven definitions of diabetes, the logistic model was used to determine odds ratios of incident diabetes for potential risk factors; an interaction term between sex and each risk factor was tested, and a P value < 0.05 used for statistical significance. In consequence, sex specific odds ratios are given for smoking and diabetes in the family, for all definitions of diabetes. The linearity of continuous risk factors was checked by the inclusion of a squared term.

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The D.E.S.I.R. diabetes risk score (2) predicts incident diabetes, and was derived for diabetes defined by FPG 7.0 mmol/l and/or treatment. This score includes for men, waist circumference, hypertension and current smoking, and for women, waist circumference, hypertension and family history of diabetes; the scoring of these attributes is as shown in the Online Appendix Table A1. Individuals can have a score between 0 and 5. The discriminative ability of this score was evaluated for each definition of diabetes, using the area under the receiver operating characteristic curve (AROC), and the 95% confidence interval.

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Supplementary Table 1. ***The D.E.S.I.R. diabetes risk score (2).***

	Men	Women
Waist circumference		
70-79 cm	0	1
80-89 cm	1	2
90-99 cm	2	3
110 cm	3	3
Current smoker	1	0
Diabetes in the family	0	1
Hypertension	1	1

Supplementary Table 2. Characteristics of men and women (mean (SD) or %), not treated for diabetes at baseline, according to whether or not they were treated for incident diabetes over the 9 years of follow-up: the D.E.S.I.R. study.

	Men			Women		
	treatment for diabetes over the 9 year follow-up			treatment for diabetes over the 9 year follow-up		
	yes	no	*P*	yes	no	*P*
	n=70	n=1826		n=38	n=1938	
Age (years)	53 (9)	47 (10)	<0.0001	55 (8)	47 (10)	0.0001
Diabetes in family	26%	18%	0.1170	45%	20%	0.0001
Current smoker	43%	25%	0.0007	5%	13%	0.1499
Alcohol (g/day)						
zero	8%	12%	0.0033	39%	37%	0.4860
0-19	13%	24%		45%	37%	
20-39	49%	49%		16%	25%	
40	30%	15%		0%	1%	
Sedentary	36%	25%	0.0381	34%	25%	0.1801
Waist (cm)	101 (9)	89 (9)	<0.0001	93 (11)	76 (10)	0.0001
BMI (kg/m²)	29.2 (3.6)	25.1 (3.0)	<0.0001	30.1 (5.3)	23.8 (3.8)	0.0001
Hypertension	84%	40%	<0.0001	66%	28%	<0.0001
Lipid treatment	20%	7%	0.0001	18%	7%	0.006

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Supplementary Table 3. Characteristics (mean (SD) or %) of those with incident diabetes, according to the seven definitions of diabetes: the D.E.S.I.R. Study

MEN		Definitions of incident diabetes					
	treatment	FPG 7.0mmol/l	HbA1c 6.5%	FPG 7.0mmol/l &/or HbA1c 6.5%	FPG 7.0mmol/l &/or treatment	HbA1c 6.5% &/or treatment	FPG 7.0mmol/l &/or HbA1c 6.5 % &/or treatment
Numbers of incident diabetes cases/N	70/1896	119/1846	74/1849	150/1857	140/1867	99/1874	171/1878
% incidence (95% CI)	3.7% (2.8-4.7)	6.4% (5.3-7.8)	4.0% (3.1-5.1)	8.1% (6.8-9.5)	7.5% (6.3-8.9)	5.3% (4.2-6.5)	9.1% (7.7-10.6)
Age (years)	53 (9)	50 (9)	52 (10)	51 (9)	50 (9)	53 (9)	51 (9)
Diabetes in family	26%	18%	23%	21%	20%	25%	22%
Current smoker	43%	38%	32%	35%	37%	34%	35%
Alcohol (g/day)							
zero	8%	11%	11%	11%	11%	10%	11%
0-19	13%	19%	15%	16%	18%	15%	16%
20-39	49%	41%	39%	45%	43%	44%	46%
40	30%	29%	35%	28%	28%	31%	27%
Sedentary	36%	30%	45%	35%	31%	42%	36%
Waist (cm)	101 (9)	95 (10)	97 (10)	96 (10)	96 (10)	98 (10)	96 (10)
BMI (kg/m²)	29.2 (3.6)	27.4 (4.0)	28.1 (4.3)	27.4 (3.9)	27.5 (4.0)	28.3 (4.1)	27.6 (3.9)
Hypertension	84%	59%	66%	59%	62%	72%	63%
Lipid treatment	20%	14%	20%	14%	14%	17%	13%

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WOMEN		Definitions of incident diabetes					
	treatment	FPG 7.0mmol/l	HbA1c 6.5%	FPG 7.0mmo/l &/or HbA1c 6.5%	FPG 7.0mmol/l &/or treatment	HbA1c 6.5% &/or treatment	FPG 7.0mmol/l, &/or HbA1c 6.% &/or treatment
Numbers of incident diabetes cases/N	38/1976	49/1944	52/1940	78/1943	63/1958	66/1954	93/1958
% incidence (95% CI)	1.9% (1.3-2.7)	2.5% (1.8-3.4)	2.7% (2.0-3.6)	4.0% (3.1-5.1)	3.2% (2.4-4.2)	3.4% (2.6-4.3)	4.7% (3.8-5.9)
Age (years)	55 (8)	50 (8)	56 (7)	53(9)	51 (8)	55 (8)	53 (8)
Diabetes in family	45%	45%	27%	33%	43%	30%	33%
Current smoker	5%	18%	15%	18%	16%	14%	16%
Alcohol (g/day)							
zero	39%	24%	44%	34%	29%	43%	38%
0-19	45%	47%	35%	40%	44%	36%	38%
20-39	16%	29%	21%	26%	27%	21%	24%
40	0%	0%	0%	0%	0%	0%	0%
Sedentary	34%	29%	35%	29%	35%	36%	33%
Waist (cm)	93 (11)	89 (12)	89 (11)	88 (11)	90(12)	90 (11)	89 (11)
BMI (kg/m²)	30.1 (5.3)	28.9 (5.5)	28.5 (5.7)	28.1 (5.2)	29.2 (5.1)	28.9 (5.4)	28.4 (5.0)
Hypertension	66%	61%	60%	60%	62%	65%	62%
Lipid treatment	18%	10%	19%	14%	14%	20%	16%

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Supplementary Table 4. Comparison (mean (SD) or %) of the 37 people with incident diabetes by HbA1c alone, with the 76 by F¨PG alone; these individuals are the same for the comparison FPG and/or treatment and HbA1c and /or treatment: the D.E.S.I.R. Study

	FPG <7.0mmol/l & HbA1c 6.5%	FPG 7.0mmol/l & HbA1c <6.5%	*P*
	n = 37	n = 76	
Women †	65%	22%	0.0001
Age (years) #	57 (10)	49 (9)	0.0001
Diabetes in family	16%	25%	0.4
Current smoker	28%	28%	0.97
Alcohol abstainer	35%	12%	0.005
Sedentary	45%	27%	0.09
Waist (cm)§ men	95 (9)	93 (9)	0.6
women	83 (11)	88 (11)	0.2
BMI (kg/m²)	26.1 (4.2)	26.4 (4.0)	0.7
Hypertension	43%	53%	0.4
Lipid treatment	16%	7%	0.2

† not adjusted

adjusted for sex

§ adjusted for age

others variables adjusted for age & sex

Supplementary Figure 1. Mean values at baseline of fasting plasma glucose and HbA1c by age class, in men and women from the D.E.S.I.R. study, who were not treated for diabetes. The difference was constant over age classes for fasting plasma glucose ($P_{interaction} = 0.6$), but not for HbA1c ($P_{interaction} = 0.0001$)

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